

WHAT IS CLAIMED IS:

1. A purified or isolated nucleic acid sequence consisting essentially of one of SEQ ID NOs: 405-485, wherein said nucleic acid inhibits microorganism proliferation.

5 2. The nucleic acid sequence of Claim 1, wherein said nucleic acid sequence is complementary to at least a portion of a coding sequence of a gene whose expression is required for microorganism proliferation.

3. The nucleic acid sequence of Claims 1 or 2, wherein said nucleic acid comprises a fragment of one of SEQ ID NOs. 405-485, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30,
10 at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.

4. The nucleic acid sequence of Claim 3, wherein said nucleic acid sequence is complementary to a coding sequence of a gene whose expression is required for microorganism proliferation.

15 5. A vector comprising a promoter operably linked to a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 405-485.

6. The vector of Claim 5, wherein said promoter is active in an organism selected from the group consisting of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*,
20 *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

7. A host cell containing the vector of Claim 5 or Claim 6.

8. A purified or isolated nucleic acid consisting essentially of the coding
30 sequence of one of SEQ ID NOs: 82-88, 90-242.

9. A fragment of the nucleic acid of Claim 8, said fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.

5 10. A vector comprising a promoter operably linked to the nucleic acid of Claim 8 or Claim 9.

11. A purified or isolated nucleic acid comprising a nucleic acid sequence complementary to at least a portion of an intragenic sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noncoding region within an operon encoding a polypeptide comprising a sequence
10 selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

12. A purified or isolated nucleic acid comprising a nucleic acid having at least 70% homology to a sequence selected from the group consisting of SEQ ID NOs 405-485, 82-88, 90-242 or the sequences complementary thereto as determined using BLASTN version 2.0 with the default parameters.

15 13. The nucleic acid of Claim 12, wherein said nucleic acid is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*,
20 *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

25 14. A purified or isolated nucleic acid consisting essentially of a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

15 15. A vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

16. A host cell containing the vector of Claim 15.

17. A purified or isolated polypeptide comprising the sequence of one of SEQ ID NOs: 243-357, 359-398.

18. A purified or isolated polypeptide comprising a fragment of one of the polypeptides of SEQ ID NOs. 243-357, 359-398, said fragment selected from the group consisting of fragments comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the polypeptides of SEQ ID NOs.: 243-357, 359-398.

19. An antibody capable of specifically binding the polypeptide of Claim 17 or Claim 18.

20. A method of producing a polypeptide, comprising introducing a vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 into a cell.

21. The method of Claim 20, further comprising the step of isolating said protein.

22. A method of inhibiting proliferation comprising inhibiting the activity or reducing the amount of a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 or inhibiting the activity or reducing the amount of a nucleic acid encoding said polypeptide.

23. A method for identifying compounds which influence the activity of a polypeptide required for proliferation comprising:

contacting a polypeptide having a sequence selected from the group consisting of 243-357, 359-398 with a candidate compound; and

determining whether said compound influences the activity of said polypeptide.

24. The method of Claim 23, wherein said activity is an enzymatic activity.

25. The method of Claim 23, wherein said activity is a carbon compound catabolism activity.

26. The method of Claim 23, wherein said activity is a biosynthetic activity.

27. The method of Claim 23, wherein said activity is a transporter activity.

28. The method of Claim 23, wherein said activity is a transcriptional activity.

29. The method of Claim 23, wherein said activity is a DNA replication activity.

30. The method of Claim 23, wherein said activity is a cell division activity.

31. A method for assaying compounds for the ability to reduce the activity or
5 level of a polypeptide required for proliferation, comprising:

providing a target, wherein said target comprises the coding sequence of
a sequence selected from the group consisting of SEQ ID NOs. 82-88, 90-242;
contacting said target with a candidate compound; and
measuring an activity of said target.

10 32. The method of Claim 31, wherein said target is a messenger RNA molecule transcribed from a coding region of one of SEQ ID. NOs.: 82-88, 90-242 and said activity is translation of said messenger RNA.

33. The method of Claim 32, wherein said target is a coding region of one of
SEQ ID. NOs. 82-88, 90-242 and said activity is transcription of said messenger RNA.

15 34. A compound identified using the method of Claim 31.

35. A method for identifying compounds which reduce the activity or level
of a gene product required for cell proliferation comprising the steps of:

expressing an antisense nucleic acid against a nucleic acid encoding said
gene product in a cell to reduce the activity or amount of said gene product in
said cell, thereby producing a sensitized cell;

20 contacting said sensitized cell with a compound; and

determining whether said compound inhibits the growth of said
sensitized cell to a greater extent than said compound inhibits the growth of a
nonsensitized cell.

25 36. The method of Claim 35, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

37. The method of Claim 36, wherein said cell is an *E. coli* cell.

30 38. The method of Claim 36, wherein said cell is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus*

5 *fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

39. The method of Claim 35, wherein said antisense nucleic acid is transcribed from an inducible promoter.

10 40. The method of Claim 39, further comprising the step of contacting said cell with a concentration of inducer which induces said antisense nucleic acid to a sublethal level.

41. The method of Claim 40, wherein said sub-lethal concentration of said inducer is such that growth inhibition is 8% or more.

42. The method of Claim 40, wherein said inducer is isopropyl-1-thio- β -D-galactoside.

15 43. The method of Claim 35, wherein growth inhibition is measured by monitoring optical density of a culture growth solution.

44. The method of Claim 35, wherein said gene product is a polypeptide.

45. The method of Claim 35, wherein said gene product is an RNA.

20 46. The method of Claim 44, wherein said gene product comprises a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

47. A compound identified using the method of Claim 35.

25 48. A method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242 or with activity against the product of said gene into a population of cells expressing a gene.

49. The method of Claim 48, wherein said compound is an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 405-485, or a proliferation-inhibiting portion thereof.

30 50. The method of Claim 49, wherein said proliferation inhibiting portion of one of SEQ ID NOs. 405-485 is a fragment comprising at least 10, at least 20, at least

25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.

51. The method of Claim 48, wherein said compound is a triple helix oligonucleotide.

5 52. A preparation comprising an effective concentration of an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 405-485, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier.

10 53. The preparation of Claim 52, wherein said proliferation-inhibiting portion of one of SEQ ID NOs. 405-485 comprises at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.

15 54. A method for inhibiting the expression of a gene in an operon required for proliferation comprising contacting a cell in a cell population with an antisense nucleic acid, said cell expressing a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242, wherein said antisense nucleic acid comprises at least a proliferation-inhibiting portion of said operon in an antisense orientation that is effective in inhibiting expression of said gene.

20 55. The method of Claim 54, wherein said antisense nucleic acid is complementary to a sequence of a gene comprising one or more of SEQ ID NOs.: 82-88, 90-242.

56. The method of Claim 54, wherein said antisense nucleic acid is a sequence of one of SEQ ID NOs.: 405-485, or a portion thereof.

25 57. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a plasmid which expresses said antisense nucleic acid into said cell population.

58. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a phage which expresses said antisense nucleic acid into said cell population.

30 59. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a sequence encoding said antisense nucleic acid into the chromosome of said cell into said cell population.

60. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a retron which expresses said antisense nucleic acid into said cell population.

5 61. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a ribozyme into said cell-population, wherein a binding portion of said ribozyme is complementary to said antisense oligonucleotide.

62. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a liposome comprising said antisense oligonucleotide into said cell.

10 63. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by electroporation.

64. The method of Claim 54, wherein said antisense nucleic acid is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.

15 65. The method of Claim 54 wherein said antisense nucleic acid is an oligonucleotide.

66. A method for identifying bacterial strains comprising the steps of:
providing a sample containing a bacterial species; and

identifying a bacterial species using a species specific probe having a
20 sequence selected from the group consisting of SEQ ID NOs. 405-485, 82-88, 90-242.

67. A method for identifying a gene in a microorganism required for proliferation comprising:

(a) identifying an inhibitory nucleic acid which inhibits the activity
25 of a gene or gene product required for proliferation in a first microorganism;

(b) contacting a second microorganism with said inhibitory nucleic acid;

(c) determining whether said inhibitory nucleic acid from said first microorganism inhibits proliferation of said second microorganism; and

30 (d) identifying the gene in said second microorganism which is inhibited by said inhibitory nucleic acid.

68. A method for assaying a compound for the ability to inhibit proliferation of a microorganism comprising:

(a) identifying a gene or gene product required for proliferation in a first microorganism;

5 (b) identifying a homolog of said gene or gene product in a second microorganism;

(c) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said second microorganism;

10 (d) contacting said second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;

(e) contacting the sensitized microorganism of step (d) with a compound; and

15 (f) determining whether said compound inhibits proliferation of said sensitized microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized microorganism.

69. The method of Claim 68, wherein said step of identifying a gene involved in proliferation in a first microorganism comprises:

20 introducing a nucleic acid comprising a random genomic fragment from said first microorganism operably linked to a promoter wherein said random genomic fragment is in the antisense orientation; and

25 comparing the proliferation of said first microorganism transcribing a first level of said random genomic fragment to the proliferation of said first microorganism transcribing a lower level of said random genomic fragment, wherein a difference in proliferation indicates that said random genomic fragment comprises a gene involved in proliferation.

30 70. The method of Claim 69, wherein said step of identifying a homolog of said gene in a second microorganism comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in a database using an algorithm selected from the group consisting of BLASTN version 2.0 with the default parameters and FASTA version 3.0t78 algorithm with the default parameters.

71. The method of Claim 69, wherein said step of identifying a homolog of said gene in a second microorganism comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide by identifying nucleic acids which hybridize to said first gene.

5 72. The method of Claim 69, wherein the step of identifying a homolog of said gene in a second microorganism comprises expressing a nucleic acid which inhibits the proliferation of said first microorganism in said second microorganism.

73. The method of Claim 69, wherein said inhibitory nucleic acid is an antisense nucleic acid.

10 74. The method of Claim 69, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of said homolog.

75. The method of Claim 69, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding said homolog.

15 76. The method of Claim 69, wherein the step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence comprises directly contacting said second microorganism with said nucleic acid.

20 77. The method of Claim 69, wherein the step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence comprises expressing an antisense nucleic acid to said homolog in said second microorganism.

78. A compound identified using the method of Claim 68.

79. A method of assaying a compound for the ability to inhibit proliferation comprising:

25 (a) identifying an inhibitory nucleic acid sequence which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;

(b) contacting a second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;

30 (c) contacting the proliferation-inhibited microorganism of step (b) with a compound; and

(d) determining whether said compound inhibits proliferation of said sensitized second microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized second microorganism.

5 80. The method of Claim 79, wherein said inhibitory nucleic acid is an antisense nucleic acid which inhibits the proliferation of said first microorganism.

81. The method of Claim 79, wherein said inhibitory nucleic acid comprises a portion of an antisense nucleic acid which inhibits the proliferation of said first microorganism.

10 82. The method of Claim 79, wherein said inhibitory nucleic acid comprises an antisense molecule against the entire coding region of the gene involved in proliferation of the first microorganism.

83. The method of Claim 79, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding the gene involved in proliferation of the first microorganism.

15 84. A compound identified using the method of Claim 79.

85. A method for assaying compounds for activity against a biological pathway required for proliferation comprising:

20 sensitizing a cell by expressing an antisense nucleic acid against a nucleic acid encoding a gene product required for proliferation in a cell to reduce the activity or amount of said gene product;

contacting the sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

25 86. The method of Claim 85, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

87. The method of Claim 86, wherein said cell is an *E. coli* cell.

30 88. The method of Claim 85, wherein said cell is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus*

fumigatus, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae*
5 or any species falling within the genera of any of the above species.

89. The method of Claim 85, wherein said antisense nucleic acid is transcribed from an inducible promoter.

90. The method of Claim 89, further comprising contacting the cell with an agent which induces expression of said antisense nucleic acid from said inducible
10 promoter, wherein said antisense nucleic acid is expressed at a sublethal level.

91. The method of Claim 90, wherein said sublethal level of said antisense nucleic acid inhibits proliferation by 8% or more.

92. The method of Claim 90, wherein said agent is isopropyl-1-thio- β -D-galactoside (IPTG).

93. The method of Claim 91, wherein inhibition of proliferation is measured
15 by monitoring the optical density of a liquid culture.

94. The method of Claim 85, wherein said gene product comprises a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

95. A compound identified using the method of Claim 85.
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96. A method for assaying a compound for the ability to inhibit cellular proliferation comprising:

contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell;

contacting said cell with said compound; and
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determining whether said compound reduces proliferation to a greater extent than said compound reduces proliferation of cells which have not been contacted with said agent.

97. The method of Claim 96, wherein said agent which reduces the activity
30 or level of a gene product required for proliferation of said cell comprises an antisense nucleic acid to a gene or operon required for proliferation.

98. The method of Claim 96, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises an antibiotic.

5 99. The method of Claim 96, wherein said cell contains a temperature sensitive mutation which reduces the activity or level of said gene product required for proliferation of said cell.

100. The method of Claim 99, wherein said antisense nucleic acid is directed against the nucleic acid encoding the same functional domain of said gene product required for proliferation of said cell to which said antisense nucleic acid is directed.

10 101. The method of Claim 99, wherein said antisense nucleic acid is directed against the nucleic acid a different functional domain of said gene product required for proliferation of said cell than the functional domain to which said antisense nucleic acid is directed.

102. A compound identified using the method of Claim 96.

15 103. A method for identifying the pathway in which a proliferation-required nucleic acid or its gene product lies comprising:

expressing a sublethal level of an antisense nucleic acid directed against said proliferation-required nucleic acid in a cell;

contacting said cell with an antibiotic, wherein the biological pathway on which said antibiotic acts is known; and

20 determining whether said cell has a substantially greater sensitivity to said antibiotic than a cell which does not express said sublethal level of said antisense nucleic acid.

104. A method for determining the pathway on which a test compound acts comprising:

25 (a) expressing a sublethal level of an antisense nucleic acid directed against a proliferation-required nucleic acid in a cell, wherein the biological pathway in which said proliferation-required nucleic acid lies is known,

(b) contacting said cell with said test compound; and

30 (c) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said antisense nucleic acid.

105. The method of Claim 104, further comprising:

(d) expressing a sublethal level of a second antisense nucleic acid directed against a second proliferation-required nucleic acid in said cell, wherein said second proliferation-required nucleic acid is in a different biological pathway than said proliferation-required nucleic acid in step (a); and

5 (e) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said second antisense nucleic acid.

106. A purified or isolated nucleic acid consisting essentially of one of SEQ ID NOs: 358, 399-402.

10 107. A compound identified using the method of Claim 23.

108. A compound which interacts with the gene or gene product of a nucleic acid comprising a sequence of one of SEQ ID NOs: 82-88, 90-242 to inhibit proliferation.

15 109. A compound which interacts with a polypeptide comprising one of SEQ ID NOs. 243-357, 359-398 to inhibit proliferation.

110. A compound which interacts with a nucleic acid comprising one of SEQ ID NOs: 358, 399-402 to inhibit proliferation.

111. A compound which interacts with a nucleic acid comprising one of SEQ ID NOs: 358, 399-402 to inhibit proliferation.